

# SEQUENCE LISTING

<110> Wolfram, Lawrence  
Letterio, John

<120> FUNCTIONALIZED TGF-BETA FUSION PROTEINS

<130> 4239-61302

<150> 60/242,292

<151> 2000-10-20

<160> 39

<170> PatentIn version 3.1

<210> 1

<211> 28

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28

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42

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48

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<213> synthetic oligopeptide

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Asp Tyr Lys Asp Asp Asp Asp Lys  
1 5

<210> 8  
<211> 1197  
<212> DNA  
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<223> Maturation cleavage site

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1 5 10 15

tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga ctg tcc acc 96  
Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
20 25 30

tgc aag acc atc gac atg gag ctg ctg aag cgg aag cgc atc gag gcc 144  
Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc ccc ccg agc 192  
Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta ctg gct ctt 240  
Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc gaa ccg gag 288  
Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc cgc gtg cta	336
Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu	
100 105 110	
atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag ggc acc ccc	384
Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro	
115 120 125	
cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg gaa gcg gtg	432
His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val	
130 135 140	
ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg ctg agg ctc	480
Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu	
145 150 155 160	
aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa tac agc aat	528
Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn	
165 170 175	
gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc agt gac tca	576
Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser	
180 185 190	
ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg cag tgg ctg	624
Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu	
195 200 205	
acc cgc aga gag gct ata gag ggt ttt cgc ctc agt gcc cac tct tcc	672
Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser	
210 215 220	
tct gac agc aaa gat aac aca ctc cac gtg gaa att aac ggg ttc aat	720
Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn	
225 230 235 240	
tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg aac cgg ccc	768
Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro	
245 250 255	
ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag cac ctg cac	816
Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His	
260 265 270	
agc tcc cgg cac cgc cga gac tac aag gat gac gac gac aag gcc ctg	864
Ser Ser Arg His Arg Arg Asp Tyr Lys Asp Asp Asp Lys Ala Leu	
275 280 285	
gat acc aac tac tgc ttc agc tcc acg gag aag aac tgc tgc gtg cgg	912
Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg	
290 295 300	
cag ctc tac att gac ttc cgg aag gac ctg ggc tgg aag tgg att cat	960
Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His	
305 310 315 320	
gaa ccc aag ggc tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc tac	1008
Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr	
325 330 335	

atc tgg agc cta gac act cag tac agc aag gtc ctg gct ctg tac aac 1056  
 ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn  
 340 345 350

cag cac aac ccg ggc gcg tcg gcg gcg ccg tgc tgc gtg ccg cag gcg 1104  
 Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala  
 355 360 365

ctg gag cca ctg ccc atc gtg tac tac gtg ggc cgc aag ccc aag gtg 1152  
 Leu Glu Pro Leu Pro ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val  
 370 375 380

gag cag ctg tcc aac atg atc gtg cgt tcc tgc aag tgc agc tga 1197  
 Glu Gln Leu Ser Asn Met ile Val Arg Ser Cys Lys Cys Ser  
 385 390 395

<210> 9  
 <211> 398  
 <212> PRT  
 <213> fusion

<220>  
 <221> misc\_feature  
 <222> (278)..(279)  
 <223> Maturation cleavage site

<400> 9

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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
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Cys Lys Thr ile Asp Met Glu Leu Val Lys Arg Lys Arg ile Glu Ala  
 35 40 45

ile Arg Gly Gln ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
 50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
 100 105 110

Met Val Glu Ser Gly Asn Gln ile Tyr Asp Lys Phe Lys Gly Thr Pro  
 115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser  
210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu  
275 280 285

Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg  
290 295 300

Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His  
305 310 315 320

Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr  
325 330 335

Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn  
340 345 350

Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala  
355 360 365

Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val

Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser  
 385 390 395

<210> 10  
 <211> 362  
 <212> DNA  
 <213> fusion

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 aagaactgct gcgtgcggca gctctacatt gacttccgga aggacctggg ctggaagtgg 120  
 attcatgaac ccaagggctc catgcccaatt tctgcctggg gccctgtccc tacatctgga 180  
 gcctagacac tcagtacagc aaggctcctgg ctctgtacaa ccagcacaac ccgggcgcggt 240  
 cggcgggcgcc gtgctgcgtg ccgcaggcgc tggagccact gcccatcgtg tactacgtgg 300  
 gccgcaagcc caaggtggag cagctgtcca acatgatcgt gcgttcctgc aagtgcagct 360  
 ga 362

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 <211> 120  
 <212> PRT  
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<220>  
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 <222> (1)..(8)  
 <223> FLAG tag

<400> 11

Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe  
 1 5 10 15

Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe  
 20 25 30

Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His  
 35 40 45

Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr  
 50 55 60

Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala  
 65 70 75 80

Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile  
85 90 95

Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met  
100 105 110

Ile Val Arg Ser Cys Lys Cys Ser  
115 120

<210> 12  
<211> 1197  
<212> DNA  
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<220>  
<221> CDS  
<222> (1)..(1197)  
<223>

<220>  
<221> misc\_feature  
<222> (278)..(279)  
<223> Maturation cleavage site

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1 5 10 15  
tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga ctg tcc acc 96  
Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
20 25 30  
tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc atc gag gcc 144  
Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45  
att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc ccc ccg agc 192  
Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60  
cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta ctg gct ctt 240  
Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80  
tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc gaa ccg gag 288  
Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95  
ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc cgc gtg cta 336  
Pro Glu Pro Glu Ala Asp Tyr Tyr Lys Glu Val Thr Arg Val Leu  
100 105 110  
atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag ggc acc ccc 384  
Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg gaa gcg gtg His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val 130 135 140	432
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aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa tac agc aat Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn 165 170 175	528
gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc agt gac tca Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser 180 185 190	576
ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg cag tgg ctg Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu 195 200 205	624
acc cgc aga gag gct ata gag ggt ttt cgc ctc agt gcc cac tct tcc Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser 210 215 220	672
tct gac agc aaa gat aac aca ctc cac gtg gaa att aac ggg ttc aat Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn 225 230 235 240	720
tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg aac cgg ccc Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro 245 250 255	768
ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag cac ctg cac Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His 260 265 270	816
agc tcc cgg cac cgc cga gcc ctg gat acc aac tac tgc ttc agc tcc Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser 275 280 285	864
acg gac tac aag gat gac gac gac aag gag aag aac tgc tgc gtg cgg Thr Asp Tyr Lys Asp Asp Asp Asp Lys Glu Lys Asn Cys Cys Val Arg 290 295 300	912
cag ctc tac att gac ttc cgg aag gac ctg ggc tgg aag tgg att cat Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His 305 310 315 320	960
gaa ccc aag ggc tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc tac Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr 325 330 335	1008
atc tgg agc cta gac act cag tac agc aag gtc ctg gct ctg tac aac Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn 340 345 350	1056
cag cac aac ccg ggc gcg tcg gcg gcg ccg tgc tgc gtg ccg cag gcg Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala 355 360 365	1104



ctg gag cca ctg ccc atc gtg tac tac gtg ggc cgc aag ccc aag gtg 1152  
 Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val  
 370 375 380

gag cag ctg tcc aac atg atc gtg cgt tcc tgc aag tgc agc tga 1197  
 Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser  
 385 390 395

<210> 13  
 <211> 398  
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 <223> Maturation cleavage site

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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
 35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
 50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
 100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
 115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
 130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
 145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser  
210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser  
275 280 285

Thr Asp Tyr Lys Asp Asp Asp Asp Lys Glu Lys Asn Cys Cys Val Arg  
290 295 300

Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His  
305 310 315 320

Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr  
325 330 335

Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn  
340 345 350

Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala  
355 360 365

Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val  
370 375 380

Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser  
385 390 395

<210> 14

<211> 362  
 <212> DNA  
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 attcatgaac ccaagggcta ccatgccaat ttctgcctgg ggccctgtcc ctacatctgg 180  
 agcctagaca ctcagtacac aaggtcctgg ctctgtacaa ccagcacaac ccggg'gcgct 240  
 cggcggcgcc gtgctgcgtg ccgcaggcgc tggagccact gcccatcgtg tactacgtgg 300  
 gccgcaagcc caaggtggag cagctgtcca acatgatcgt gcgttctgc aagtgcagct 360  
 ga 362

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 <221> peptide  
 <222> (12)..(19)  
 <223> FLAG tag

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Asp Asp Lys Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe  
 20 25 30

Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His  
 35 40 45

Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr  
 50 55 60

Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala  
 65 70 75 80

Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile  
 85 90 95

Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met  
 100 105 110

Ile Val Arg Ser Cys Lys Cys Ser  
 115 120

<210> 16  
 <211> 1612  
 <212> DNA  
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 <222> (348)..(1559)  
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 <222> (1560)..(1612)  
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<220>  
 <221> misc\_feature  
 <222> (1197)..(1220)  
 <223> Encodes FLAG epitope tag

<220>  
 <221> misc\_feature  
 <222> (1182)..(1159)  
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 agagcgctca tctcgatttt taccctggtg gtatactgag acaccttggt gtcagagcct 180  
 caccgcgact cctgctgctt tctccctcaa cctcaaatta ttcaggacta tcacctacct 240  
 ttccttgga gacccaccc cacaagccct gcaggggcgg ggccctcgca tccaccttt 300  
 gccgaggggt cccgctctcc gaagtgcctg ggggcgcgc ctcccc atg ccg ccc 356  
 Met Pro Pro  
 1  
 tcg ggg ctg cgg cta ctg ccg ctt ctg ctc cca ctc ccg tgg ctt cta 404

Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro Trp Leu Leu  
 5 10 15

gtg ctg acg ccc ggg agg cca gcc gcg gga ctc tcc acc tgc aag acc 452  
 Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr 35  
 20 25 30

atc gac atg gag ctg gtg aaa cgg aag cgc atc gaa gcc atc cgt ggc 500  
 Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala Ile Arg Gly 50  
 40 45

cag atc ctg tcc aaa cta agg ctc gcc agt ccc cca agc cag ggg gag 548  
 Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu 65  
 55 60

gta ccg ccc ggc ccg ctg ccc gag gcg gtg ctc gct ttg tac aac agc 596  
 Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser 80  
 70 75

acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccg gag ccc 644  
 Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro 95  
 85 90

gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac 692  
 Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp 115  
 100 105 110

cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata 740  
 Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 130  
 120 125

tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc 788  
 Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro 145  
 135 140

cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt 836  
 Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 160  
 150 155

gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg 884  
 Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp 175  
 165 170

cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg 932  
 Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp 195  
 180 185 190

ctg tct ttt gac gtc act gga gtt gta cgg cag tgg ctg aac caa gga 980  
 Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu Asn Gln Gly 210  
 200 205

gac gga ata cag ggc ttt cga ttc agc gct cac tgc tct tgt gac agc 1028  
 Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser Cys Asp Ser 225  
 215 220

aaa gat aac aaa ctc cac gtg gaa atc aac ggg atc agc ccc aaa cgt 1076  
 Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser Pro Lys Arg 240  
 230 235

cgg ggc gac ctg ggc acc atc cat gac atg aac cgg ccc ttc ctg ctc 1124  
 Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro Phe Leu Leu

245

250

255

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ctc atg gcc acc ccc ctg gaa agg gcc cag cac ctg cac agc tca cgg      1172
Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His Ser Ser Arg
260                      265                      270                      275

cac cgg aga gcc ctg gat acc aac gac tac aag gat gac gac gac aag      1220
His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp Asp Asp Lys
                      280                      285                      290

gcc ctg gat acc aac tat tgc ttc agc tcc aca gag aag aac tgc tgt      1268
Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys
                      295                      300                      305

gtg cgg cag ctg tac att gac ttt agg aag gac ctg ggt tgg aag tgg      1316
Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp
                      310                      315                      320

atc cac gag ccc aag ggc tac cat gcc aac ttc tgt ctg gga ccc tgc      1364
Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys
                      325                      330                      335

ccc tat att tgg agc ctg gac aca cag tac agc aag gtc ctt gcc ctc      1412
Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu
340                      345                      350                      355

tac aac caa cac aac ccg ggc gct tcg gcg tca ccg tgc tgc gtg ccg      1460
Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ser Pro Cys Cys Val Pro
                      360                      365                      370

cag gct ttg gag cca ctg ccc atc gtc tac tac gtg ggt cgc aag ccc      1508
Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro
                      375                      380                      385

aag gtg gag cag ttg tcc aac atg att gtg cgc tcc tgc aag tgc agc      1556
Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser
                      390                      395                      400

tga agccccgcc cgcgccgcc ctcccggcag gcccgcccc gcccccgcc cgc      1612

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<220>  
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 <222> (1197)..(1220)  
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<220>  
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Met Pro Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro  
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20 25 30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser  
115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val  
130 135 140

Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu  
145 150 155 160

Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser  
210 215 220

Cys Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser  
225 230 235 240

Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp  
275 280 285

Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys  
290 295 300

Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly  
305 310 315 320

Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu  
325 330 335

Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val  
340 345 350

Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ser Pro Cys  
355 360 365

Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly  
370 375 380

Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys  
385 390 395 400

Lys Cys Ser

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ttcagctcca cgg 73

<210> 19  
<211> 72



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caggtgctgg gc 72

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agagcgctca tctcgatttt taccctggtg gtatactgag acaccttggg gtcagagcct 180  
caccgcgact cctgctgctt tctccctcaa cctcaaatta ttcaggacta tcacctacct 240

ttccttggga gacccccaccc cacaagccct gcaggggcg	ggcctccgca tcccaccttt	300
gccgaggggtt cccgctctcc gaagtgccgt ggggcgccgc	ctcccc atg ccg ccc	356
	Met Pro Pro	
	1	
tcg ggg ctg cgg cta ctg ccg ctt ctg ctc cca ctc ccg tgg ctt cta		404
Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro	Leu Pro Trp Leu Leu	
5	10 15	
gtg ctg acg ccc ggg agg cca gcc gcg gga ctc tcc acc tgc aag acc		452
Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr		
20	25 30 35	
atc gac atg gag ctg gtg aaa cgg aag cgc atc gaa gcc atc cgt ggc		500
Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala Ile Arg Gly		
	40 45 50	
cag atc ctg tcc aaa cta agg ctc gcc agt ccc cca agc cag ggg gag		548
Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu		
	55 60 65	
gta ccg ccc ggc ccg ctg ccc gag gcg gtg ctc gct ttg tac aac agc		596
Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser		
	70 75 80	
acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccg gag ccc		644
Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro		
	85 90 95	
gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac		692
Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp		
	100 105 110 115	
cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata		740
Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile		
	120 125 130	
tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc		788
Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro		
	135 140 145	
cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt		836
Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser		
	150 155 160	
gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg		884
Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp		
	165 170 175	
cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg		932
Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp		
	180 185 190 195	
ctg tct ttt gac gtc act gga gtt gta cgg cag tgg ctg aac caa gga		980
Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu Asn Gln Gly		
	200 205 210	
gac gga ata cag ggc ttt cga ttc agc gct cac tgc tct tgt gac agc		1028
Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser Cys Asp Ser		

215	220	225	
aaa gat aac aaa ctc cac gtg gaa atc aac ggg atc agc ccc aaa cgt Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser Pro Lys Arg 230 235 240			1076
cgg ggc gac ctg ggc acc atc cat gac atg aac cgg ccc ttc ctg ctc Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro Phe Leu Leu 245 250 255			1124
ctc atg gcc acc ccc ctg gaa agg gcc cag cac ctg cac agc tca cgg Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His Ser Ser Arg 260 265 270 275			1172
cac cgg aga gcc ctg gat acc aac agc tac cca tac gac gtg cca gac His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp Val Pro Asp 280 285 290			1220
tac gca tct ctg gcc ctg gat acc aac tat tgc ttc agc tcc aca gag Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu 295 300 305			1268
aag aac tgc tgt gtg cgg cag ctg tac att gac ttt agg aag gac ctg Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu 310 315 320			1316
ggt tgg aag tgg atc cac gag ccc aag ggc tac cat gcc aac ttc tgt Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys 325 330 335			1364
ctg gga ccc tgc ccc tat att tgg agc ctg gac aca cag tac agc aag Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys 340 345 350 355			1412
gtc ctt gcc ctc tac aac caa cac aac ccg ggc gct tcg gcg tca ccg Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ser Pro 360 365 370			1460
tgc tgc gtg ccg cag gct ttg gag cca ctg ccc atc gtc tac tac gtg Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val 375 380 385			1508
ggt cgc aag ccc aag gtg gag cag ttg tcc aac atg att gtg cgc tcc Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser 390 395 400			1556
tgc aag tgc agc tga agccccgccc cgccccgccc ctccccggcag gcccgcccc Cys Lys Cys Ser 405			1611
gcccccgccc cgc			1624

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<223> Encodes amino acid residues 1-5 of TGF-beta1

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<223> Encodes HA epitope tag

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<221> misc feature

<222> (1182)..(1571)

<223> Encodes mature fusion protein

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20 25 30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser  
115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val  
130 135 140

Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu  
145 150 155 160

Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asn Ser Trp Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Asn Gln Gly Asp Gly Ile Gln Gly Phe Arg Phe Ser Ala His Cys Ser  
210 215 220

Cys Asp Ser Lys Asp Asn Lys Leu His Val Glu Ile Asn Gly Ile Ser  
225 230 235 240

Pro Lys Arg Arg Gly Asp Leu Gly Thr Ile His Asp Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp  
275 280 285

Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser  
290 295 300

Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg  
305 310 315 320

Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala  
325 330 335

Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln  
340 345 350

Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser  
355 360 365

Ala Ser Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val  
370 375 380

Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile  
385 390 395 400

Val Arg Ser Cys Lys Cys Ser  
405

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<211> 108

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 accaactact gcttcagctc cacggagaag aactgctgcg tgcggcag 108

<210> 23  
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 cagagatgcg tagtctggca cgtcgtatgg gtagctgttg gtagccaggg ctgcggcggg 60  
 ccgggagctg tgc 73

<210> 24  
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 <212> DNA  
 <213> Fusion

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<220>  
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 <222> (922)..(945)  
 <223> Encodes FLAG epitope tag

<220>  
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 <222> (907)..(1284)  
 <223> Encodes mature fusion protein

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 atg cac tac tgt gtg ctg agc acc ttt ttg ctc ctg cat ctg gtc ccg 48  
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 1 5 10 15  
 gtg gcg ctc agt ctg tct acc tgc agc acc ctc gac atg gat cag ttt 96  
 Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe  
 20 25 30

atg cgc aag agg atc gag gcc atc cgc ggg cag atc ctg agc aag ctg	144
Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu	
35 40 45	
aag ctc acc agc ccc ccg gaa gac tat ccg gag ccg gat gag gtc ccc	192
Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Asp Glu Val Pro	
50 55 60	
ccg gag gtg att tcc atc tac aac agt acc agg gac tta ctg cag gag	240
Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu	
65 70 75 80	
aag gca agc cgg agg gca gcc gcc tgc gag cgc gag cgg agc gag cag	288
Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Glu Gln	
85 90 95	
gag tac tac gcc aag gag gtt tat aaa atc gac atg ccg tcc cac ctc	336
Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser His Leu	
100 105 110	
ccc tcc gaa aat gcc atc ccg ccc act ttc tac aga ccc tac ttc aga	384
Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg	
115 120 125	
atc gtc cgc ttt gat gtc tca aca atg gag aaa aat gct tcg aat ctg	432
Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu	
130 135 140	
gtg aag gca gag ttc agg gtc ttc cgc ttg caa aac ccc aaa gcc aga	480
Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg	
145 150 155 160	
gtg gcc gag cag cgg att gaa ctg tat cag atc ctt aaa tcc aaa gac	528
Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp	
165 170 175	
tta aca tct ccc acc cag cgc tac atc gat agc aag gtt gtg aaa acc	576
Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr	
180 185 190	
aga gcg gag ggt gaa tgg ctc tcc ttc gac gtg aca gac gct gtg cag	624
Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln	
195 200 205	
gag tgg ctt cac cac aaa gac agg aac ctg ggg ttt aaa ata agt tta	672
Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu	
210 215 220	
cac tgc ccc tgc tgt acc ttc gtg ccg tct aat aat tac atc atc ccg	720
His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro	
225 230 235 240	
aat aaa agc gaa gag ctc gag gcg aga ttt gca ggt att gat ggc acc	768
Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr	
245 250 255	
tct aca tat gcc agt ggt gat cag aaa act ata aag tcc act agg aaa	816
Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys	
260 265 270	

aaa acc agt ggg aag acc cca cat ctc ctg cta atg ttg ttg ccc tcc	864
Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser	
275 280 285	
tac aga ctg gag tca caa cag tcc agc cgg cgg aag aag cgc gct ttg	912
Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu	
290 295 300	
gat gct gcc gac tac aag gat gac gac gac aag gct ttg gat gct gcc	960
Asp Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Ala Ala	
305 310 315 320	
tac tgc ttt aga aat gtg cag gat aat tgc tgc ctt cgc cct ctt tac	1008
Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro Leu Tyr	
325 330 335	
att gat ttt aag agg gat ctt gga tgg aaa tgg atc cat gaa ccc aaa	1056
Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys	
340 345 350	
ggg tac aat gct aac ttc tgt gct ggg gca tgc cca tat cta tgg agt	1104
Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu Trp Ser	
355 360 365	
tca gac act caa cac acc aaa gtc ctc agc ctg tac aac acc ata aat	1152
Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr Asn Thr Ile Asn	
370 375 380	
ccc gaa gct tcc gct tcc cct tgc tgt gtg tcc cag gat ctg gaa cca	1200
Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu Glu Pro	
385 390 395 400	
ctg acc att ctc tat tac att gga aat acg ccc aag atc gaa cag ctt	1248
Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr Pro Lys Ile Glu Gln Leu	
405 410 415	
tcc aat atg att gtc aag tct tgt aaa tgc agc taa	1284
Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser	
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<220>  
 <221> misc\_feature  
 <222> (907)..(1284)  
 <223> Encodes mature fusion protein



<400> 25

Met His Tyr Cys Val Leu Ser Thr Phe Leu Leu Leu His Leu Val Pro  
1 5 10 15

Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe  
20 25 30

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu  
35 40 45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Asp Glu Val Pro  
50 55 60

Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu  
65 70 75 80

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Glu Gln  
85 90 95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser His Leu  
100 105 110

Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg  
115 120 125

Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu  
130 135 140

Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg  
145 150 155 160

Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp  
165 170 175

Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr  
180 185 190

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln  
195 200 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu  
210 215 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro  
225 230 235 240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr  
245 250 255

Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys  
260 265 270

Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser  
275 280 285

Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu  
290 295 300

Asp Ala Ala Asp Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Ala Ala  
305 310 315 320

Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro Leu Tyr  
325 330 335

Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys  
340 345 350

Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu Trp Ser  
355 360 365

Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr Asn Thr Ile Asn  
370 375 380

Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu Glu Pro  
385 390 395 400

Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr Pro Lys Ile Glu Gln Leu  
405 410 415

Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser  
420 425

<210> 26  
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<212> DNA  
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<220>  
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<220>  
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 gtc ccg gtg gcg ctc agt ctg tct acc tgc agc acc ctc gac atg gat 97  
 Val Pro Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp  
 15 20 25 30  
 cag ttt atg cgc aag agg atc gag gcc atc cgc ggg cag atc ctg agc 145  
 Gln Phe Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser  
 35 40 45  
 aag ctg aag ctc acc agc ccc ccg gaa gac tat ccg gag ccg gat gag 193  
 Lys Leu Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Asp Glu  
 50 55 60  
 gtc ccc ccg gag gtg att tcc atc tac aac agt acc agg gac tta ctg 241  
 Val Pro Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu  
 65 70 75  
 cag gag aag gca agc cgg agg gca gcc gcc tgc gag cgc gag cgg agc 289  
 Gln Glu Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser  
 80 85 90  
 gag cag gag tac tac gcc aag gag gtt tat aaa atc gac atg ccg tcc 337  
 Glu Gln Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser  
 95 100 105 110  
 cac ctc ccc tcc gaa aat gcc atc ccg ccc act ttc tac aga ccc tac 385  
 His Leu Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr  
 115 120 125  
 ttc aga atc gtc cgc ttt gat gtc tca aca atg gag aaa aat gct tcg 433  
 Phe Arg Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser  
 130 135 140  
 aat ctg gtg aag gca gag ttc agg gtc ttc cgc ttg caa aac ccc aaa 481

Asn	Leu	Val	Lys	Ala	Glu	Phe	Arg	Val	Phe	Arg	Leu	Gln	Asn	Pro	Lys		
	145						150					155					
gcc	aga	gtg	gcc	gag	cag	cgg	att	gaa	ctg	tat	cag	atc	ctt	aaa	tcc	529	
Ala	Arg	Val	Ala	Glu	Gln	Arg	Ile	Glu	Leu	Tyr	Gln	Ile	Leu	Lys	Ser		
	160					165					170						
aaa	gac	tta	aca	tct	ccc	acc	cag	cgc	tac	atc	gat	agc	aag	gtt	gtg	577	
Lys	Asp	Leu	Thr	Ser	Pro	Thr	Gln	Arg	Tyr	Ile	Asp	Ser	Lys	Val	Val		
	175				180					185					190		
aaa	acc	aga	gcg	gag	ggt	gaa	tgg	ctc	tcc	ttc	gac	gtg	aca	gac	gct	625	
Lys	Thr	Arg	Ala	Glu	Gly	Glu	Trp	Leu	Ser	Phe	Asp	Val	Thr	Asp	Ala		
				195					200					205			
gtg	cag	gag	tgg	ctt	cac	cac	aaa	gac	agg	aac	ctg	ggg	ttt	aaa	ata	673	
Val	Gln	Glu	Trp	Leu	His	His	Lys	Asp	Arg	Asn	Leu	Gly	Phe	Lys	Ile		
			210					215					220				
agt	tta	cac	tgc	ccc	tgc	tgt	acc	ttc	gtg	ccg	tct	aat	aat	tac	atc	721	
Ser	Leu	His	Cys	Pro	Cys	Cys	Thr	Phe	Val	Pro	Ser	Asn	Asn	Tyr	Ile		
		225					230					235					
atc	ccg	aat	aaa	agc	gaa	gag	ctc	gag	gcg	aga	ttt	gca	ggg	att	gat	769	
Ile	Pro	Asn	Lys	Ser	Glu	Glu	Leu	Glu	Ala	Arg	Phe	Ala	Gly	Ile	Asp		
	240					245					250						
ggc	acc	tct	aca	tat	gcc	agt	ggt	gat	cag	aaa	act	ata	aag	tcc	act	817	
Gly	Thr	Ser	Thr	Tyr	Ala	Ser	Gly	Asp	Gln	Lys	Thr	Ile	Lys	Ser	Thr		
	255				260					265					270		
agg	aaa	aaa	acc	agt	ggg	aag	acc	cca	cat	ctc	ctg	cta	atg	ttg	ttg	865	
Arg	Lys	Lys	Thr	Ser	Gly	Lys	Thr	Pro	His	Leu	Leu	Leu	Met	Leu	Leu		
				275					280					285			
ccc	tcc	tac	aga	ctg	gag	tca	caa	cag	tcc	agc	cgg	cgg	aag	aag	cgc	913	
Pro	Ser	Tyr	Arg	Leu	Glu	Ser	Gln	Gln	Ser	Ser	Arg	Arg	Lys	Lys	Arg		
			290					295					300				
gct	ttg	gat	gct	gcc	agc	tac	cca	tac	gac	gtg	cca	gac	tac	gca	tct	961	
Ala	Leu	Asp	Ala	Ala	Ser	Tyr	Pro	Tyr	Asp	Val	Pro	Asp	Tyr	Ala	Ser		
		305					310					315					
ctg	gct	ttg	gat	gct	gcc	tac	tgc	ttt	aga	aat	gtg	cag	gat	aat	tgc	1009	
Leu	Ala	Leu	Asp	Ala	Ala	Tyr	Cys	Phe	Arg	Asn	Val	Gln	Asp	Asn	Cys		
		320				325					330						
tgc	ctt	cgc	cct	ctt	tac	att	gat	ttt	aag	agg	gat	ctt	gga	tgg	aaa	1057	
Cys	Leu	Arg	Pro	Leu	Tyr	Ile	Asp	Phe	Lys	Arg	Asp	Leu	Gly	Trp	Lys		
		335			340					345					350		
tgg	atc	cat	gaa	ccc	aaa	ggg	tac	aat	gct	aac	ttc	tgt	gct	ggg	gca	1105	
Trp	Ile	His	Glu	Pro	Lys	Gly	Tyr	Asn	Ala	Asn	Phe	Cys	Ala	Gly	Ala		
				355					360					365			
tgc	cca	tat	cta	tgg	agt	tca	gac	act	caa	cac	acc	aaa	gtc	ctc	agc	1153	
Cys	Pro	Tyr	Leu	Trp	Ser	Ser	Asp	Thr	Gln	His	Thr	Lys	Val	Leu	Ser		
			370					375					380				
ctg	tac	aac	acc	ata	aat	ccc	gaa	gct	tcc	gct	tcc	cct	tgc	tgt	gtg	1201	
Leu	Tyr	Asn	Thr	Ile	Asn	Pro	Glu	Ala	Ser	Ala	Ser	Pro	Cys	Cys	Val		

385

390

395

tcc cag gat ctg gaa cca ctg acc att ctc tat tac att gga aat acg  
 Ser Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr  
 400 405 410

1249

ccc aag atc gaa cag ctt tcc aat atg att gtc aag tct tgt aaa tgc  
 Pro Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys  
 415 420 425 430

1297

agc taa  
 Ser

1303

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Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe  
 20 25 30

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu  
 35 40 45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Asp Glu Val Pro  
 50 55 60

Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu  
 65 70 75 80

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Glu Gln  
 85 90 95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser His Leu  
 100 105 110

Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg  
 115 120 125

Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu  
 130 135 140

Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg  
 145 150 155 160

Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp  
 165 170 175

Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr  
 180 185 190

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln  
 195 200 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu  
 210 215 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro  
 225 230 235 240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr  
 245 250 255

Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys  
 260 265 270

Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser  
 275 280 285

Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu  
 290 295 300

Asp Ala Ala Ser Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala  
 305 310 315 320

Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu  
 325 330 335

Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile

340

345

350

His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro  
 355 360 365

Tyr Leu Trp Ser Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr  
 370 375 380

Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln  
 385 390 395 400

Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Asn Thr Pro Lys  
 405 410 415

Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser  
 420 425 430

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 1 5 10 15

aca atc agc ctc tct ctg tcc act tgc acc acg ttg gac ttc ggc cac 96  
 Thr Ile Ser Leu Ser Leu Ser Thr Cys Thr Thr Leu Asp Phe Gly His  
 20 25 30

atc aag aag aag agg gtg gaa gcc att agg gga cag atc ttg agc aag	144
Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys	
35 40 45	
ctc agg ctc acc agc ccc cct gag cca tcg gtg atg acc cac gtc ccc	192
Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro	
50 55 60	
tat cag gtc ctg gca ctt tac aac agc acc cgg gag ttg ctg gaa gag	240
Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu	
65 70 75 80	
atg cac ggg gag agg gag gaa ggc tgc act cag gag acc tcg gag tct	288
Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser	
85 90 95	
gag tac tat gcc aaa gag atc cat aaa ttc gac atg atc cag gga ctg	336
Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu	
100 105 110	
gcg gag cac aat gaa ctg gcc gtc tgc ccc aaa gga att acc tct aag	384
Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys	
115 120 125	
gtt ttt cgt ttc aat gtg tcc tca gtg gag aaa aat gga acc aat ctg	432
Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu	
130 135 140	
ttc cgg gca gag ttc cgg gtc ttg cgg gtg ccc aac ccc agc tcc aag	480
Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys	
145 150 155 160	
cgc aca gag cag aga att gag ctc ttc cag ata ctt cga ccg gat gag	528
Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu	
165 170 175	
cac ata gcc aag cag cgc tac ata ggt ggc aag aat ctg ccc aca agg	576
His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg	
180 185 190	
ggc acc gct gaa tgg ctg tct ttc gat gtc act gac act gtg cgc gag	624
Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu	
195 200 205	
tgg ctg ttg agg aga gag tcc aac ttg ggt ctg gaa atc agc atc cac	672
Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His	
210 215 220	
tgt cca tgt cac acc ttt cag ccc aat gga gac ata ctg gaa aat gtt	720
Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val	
225 230 235 240	
cat gag gtg atg gaa atc aaa ttc aaa gga gtg gac aat gaa gat gac	768
His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp	
245 250 255	
cat ggc cgt gga gac ctg ggg cgt ctc aag aag caa aag gat cac cac	816
His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His	
260 265 270	
aac cca cac ctg atc ctc atg atg atc ccc cca cac cga ctg gac agc	864



Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser  
 275 280 285

cca ggc cag ggc agt cag agg aag aag agg gcc ctg gac acc aat gac 912  
 Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Asp  
 290 295 300

tac aag gat gac gac gac aag gcc ctg gac acc aat tac tgc ttc cgc 960  
 Tyr Lys Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Arg  
 305 310 315 320

aac ctg gag gag aac tgc tgt gta cgc ccc ctt tat att gac ttc cgg 1008  
 Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp Phe Arg  
 325 330 335

cag gat cta ggc tgg aaa tgg gtc cac gaa cct aag ggt tac tat gcc 1056  
 Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr Tyr Ala  
 340 345 350

aac ttc tgc tca ggc cct tgc cca tac ctc cgc agc gca gac aca acc 1104  
 Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp Thr Thr  
 355 360 365

cat agc acg gtg ctt gga cta tac aac acc ctg aac cca gag gcg tct 1152  
 His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu Ala Ser  
 370 375 380

gcc tcg cca tgc tgc gtc ccc cag gac ctg gag ccc ctg acc atc ttg 1200  
 Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro Leu Thr Ile Leu  
 385 390 395 400

tac tat gtg ggc aga acc ccc aag gtg gag cag ctg tcc aac atg gtg 1248  
 Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu Ser Asn Met Val  
 405 410 415

gtg aag tcg tgt aag tgc agc tga 1272  
 Val Lys Ser Cys Lys Cys Ser  
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 <223> Encodes amino acid residues 1-5 of TGF-beta3

<220>  
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Thr Ile Ser Leu Ser Leu Ser Thr Cys Thr Thr Leu Asp Phe Gly His  
20 25 30

Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys  
35 40 45

Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro  
50 55 60

Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu  
65 70 75 80

Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser  
85 90 95

Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu  
100 105 110

Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys  
115 120 125

Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu  
130 135 140

Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys  
145 150 155 160

Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu  
165 170 175

His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg  
180 185 190

Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu  
195 200 205

Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His  
210 215 220

Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val  
225 230 235 240

His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp  
245 250 255

His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His  
260 265 270

Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser  
275 280 285

Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Asp  
290 295 300

Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Arg  
305 310 315 320

Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp Phe Arg  
325 330 335

Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr Tyr Ala  
340 345 350

Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp Thr Thr  
355 360 365

His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu Ala Ser  
370 375 380

Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro Leu Thr Ile Leu  
385 390 395 400

Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu Ser Asn Met Val  
405 410 415

Val Lys Ser Cys Lys Cys Ser  
420

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 1 5 10 15

aca atc agc ctc tct ctg tcc act tgc acc acg ttg gac ttc ggc cac 96  
 Thr Ile Ser Leu Ser Leu Ser Thr Cys Thr Thr Leu Asp Phe Gly His  
 20 25 30

atc aag aag aag agg gtg gaa gcc att agg gga cag atc ttg agc aag 144  
 Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys  
 35 40 45

ctc agg ctc acc agc ccc cct gag cca tcg gtg atg acc cac gtc ccc 192  
 Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro  
 50 55 60

tat cag gtc ctg gca ctt tac aac agc acc cgg gag ttg ctg gaa gag 240  
 Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu  
 65 70 75 80

atg cac ggg gag agg gag gaa ggc tgc act cag gag acc tcg gag tct 288  
 Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser  
 85 90 95

gag tac tat gcc aaa gag atc cat aaa ttc gac atg atc cag gga ctg 336  
 Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu  
 100 105 110

gcg gag cac aat gaa ctg gcc gtc tgc ccc aaa gga att acc tct aag 384  
 Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys  
 115 120 125

gtt ttt cgt ttc aat gtg tcc tca gtg gag aaa aat gga acc aat ctg 432  
 Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu  
 130 135 140

ttc cgg gca gag ttc cgg gtc ttg cgg gtg ccc aac ccc agc tcc aag 480  
 Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys  
 145 150 155 160

cgc aca gag cag aga att gag ctc ttc cag ata ctt cga ccg gat gag 528  
 Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu  
 165 170 175

cac ata gcc aag cag cgc tac ata ggt ggc aag aat ctg ccc aca agg	576
His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg	
180 185 190	
ggc acc gct gaa tgg ctg tct ttc gat gtc act gac act gtg cgc gag	624
Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu	
195 200 205	
tgg ctg ttg agg aga gag tcc aac ttg ggt ctg gaa atc agc atc cac	672
Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His	
210 215 220	
tgt cca tgt cac acc ttt cag ccc aat gga gac ata ctg gaa aat gtt	720
Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val	
225 230 235 240	
cat gag gtg atg gaa atc aaa ttc aaa gga gtg gac aat gaa gat gac	768
His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp	
245 250 255	
cat ggc cgt gga gac ctg ggg cgt ctc aag aag caa aag gat cac cac	816
His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His	
260 265 270	
aac cca cac ctg atc ctc atg atg atc ccc cca cac cga ctg gac agc	864
Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser	
275 280 285	
cca ggc cag ggc agt cag agg aag aag agg gcc ctg gac acc aat agc	912
Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Ser	
290 295 300	
tac cca tac gac gtg cca gac tac gca tct ctg gcc ctg gac acc aat	960
Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn	
305 310 315 320	
tac tgc ttc cgc aac ctg gag gag aac tgc tgt gta cgc ccc ctt tat	1008
Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr	
325 330 335	
att gac ttc cgg cag gat cta ggc tgg aaa tgg gtc cac gaa cct aag	1056
Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys	
340 345 350	
ggt tac tat gcc aac ttc tgc tca ggc cct tgc cca tac ctc cgc agc	1104
Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser	
355 360 365	
gca gac aca acc cat agc acg gtg ctt gga cta tac aac acc ctg aac	1152
Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn	
370 375 380	
cca gag gcg tct gcc tcg cca tgc tgc gtc ccc cag gac ctg gag ccc	1200
Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro	
385 390 395 400	
ctg acc atc ttg tac tat gtg ggc aga acc ccc aag gtg gag cag ctg	1248
Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu	
405 410 415	
tcc aac atg gtg gtg aag tcg tgt aag tgc agc tga	1284

Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
420 425

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Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys  
35 40 45

Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro  
50 55 60

Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu  
65 70 75 80

Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser  
85 90 95

Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu  
100 105 110

Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys  
115 120 125

Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu  
130 135 140

Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys  
145 150 155 160

Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu  
165 170 175

His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg  
180 185 190

Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu  
195 200 205

Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His  
210 215 220

Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val  
225 230 235 240

His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp  
245 250 255

His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His  
260 265 270

Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser  
275 280 285

Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Ser  
290 295 300

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn  
305 310 315 320

Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr  
325 330 335

Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys  
340 345 350

Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser  
355 360 365

Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn  
370 375 380

Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu Pro  
 385 390 395 400

Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu  
 405 410 415

Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser  
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ccg ctg ctg tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga  
 Pro Leu Leu Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly  
 15 20 25

49

97



ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc	145
Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg	
30 35 40 45	
atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc	193
Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser	
50 55 60	
ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta	241
Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val	
65 70 75	
ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc	289
Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val	
80 85 90	
gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc	337
Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr	
95 100 105	
cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag	385
Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys	
110 115 120 125	
ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg	433
Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg	
130 135 140	
gaa gcg gtg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg	481
Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu	
145 150 155	
ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa	529
Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys	
160 165 170	
tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc	577
Tyr Ser Asn Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro	
175 180 185	
agt gac tca ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg	625
Ser Asp Ser Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg	
190 195 200 205	
cag tgg ctg acc cgc aga gag gct ata gag ggt ttt cgc ctc agt gcc	673
Gln Trp Leu Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala	
210 215 220	
cac tct tcc tct gac agc aaa gat aac aca ctc cac gtg gaa att aac	721
His Ser Ser Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn	
225 230 235	
ggg ttc aat tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg	769
Gly Phe Asn Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met	
240 245 250	
aac cgg ccc ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag	817
Asn Arg Pro Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln	
255 260 265	

cac ctg cac agc tcc cgg cac cgc cga gcc ctg gat acc aac gac tac 865  
 His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp Tyr  
 270 275 280 285

aag gat gac gac gac aag gcc ctg gat acc aac tac tgc ttc agc tcc 913  
 Lys Asp Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser  
 290 295 300

acg gag aag aac tgc tgc gtg cgg cag ctc tac att gac ttc cgg aag 961  
 Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys  
 305 310 315

gac ctg ggc tgg aag tgg att cat gaa ccc aag ggc tac cat gcc aat 1009  
 Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn  
 320 325 330

ttc tgc ctg ggg ccc tgt ccc tac atc tgg agc cta gac act cag tac 1057  
 Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr  
 335 340 345

agc aag gtc ctg gct ctg tac aac cag cac aac ccg ggc gcg tcg gcg 1105  
 Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala  
 350 355 360 365

gcg ccg tgc tgc gtg ccg cag gcg ctg gag cca ctg ccc atc gtg tac 1153  
 Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr  
 370 375 380

tac gtg ggc cgc aag ccc aag gtg gag cag ctg tcc aac atg atc gtg 1201  
 Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val  
 385 390 395

cgt tcc tgc aag tgc agc tga ggccccgccc cgccacagc cccgcccacc 1252  
 Arg Ser Cys Lys Cys Ser  
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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser  
210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp  
275 280 285

Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys  
290 295 300

Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly  
305 310 315 320

Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu  
325 330 335

Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val  
340 345 350

Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys  
355 360 365

Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly  
370 375 380

Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys  
385 390 395 400

Lys Cys Ser

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ctg ccg ctg ctg tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc 98  
 Leu Pro Leu Leu Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala  
 15 20 25

gga ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag 146  
 Gly Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys  
 30 35 40

cgc atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc 194  
 Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala  
 45 50 55 60

agc ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca 242  
 Ser Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala  
 65 70 75

gta ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt 290  
 Val Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser  
 80 85 90

gtc gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc 338  
 Val Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val  
 95 100 105

acc cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc 386  
 Thr Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe  
 110 115 120

aag ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc 434  
 Lys Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu  
 125 130 135 140

cgg gaa gcg gtg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc Arg Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg 145 150 155	482
ctg ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag Leu Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln 160 165 170	530
aaa tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc Lys Tyr Ser Asn Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala 175 180 185	578
ccc agt gac tca ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg Pro Ser Asp Ser Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val 190 195 200	626
cgg cag tgg ctg acc cgc aga gag gct ata gag ggt ttt cgc ctc agt Arg Gln Trp Leu Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser 205 210 215 220	674
gcc cac tgt tcc tgt gac agc aaa gat aac aca ctc cac gtg gaa att Ala His Cys Ser Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile 225 230 235	722
aac ggg ttc aat tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc Asn Gly Phe Asn Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly 240 245 250	770
atg aac cgg ccc ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc Met Asn Arg Pro Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala 255 260 265	818
cag cac ctg cac agc tcc cgg cac cgc cga gcc ctg gat acc aac gac Gln His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp 270 275 280	866
tac aag gat gac gac gac aag gcc ctg gat acc aac tac tgc ttc agc Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser 285 290 295 300	914
tcc acg gag aag aac tgc tgc gtg cgg cag ctc tac att gac ttc cgg Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg 305 310 315	962
aag gac ctg ggc tgg aag tgg att cat gaa ccc aag ggc tac cat gcc Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala 320 325 330	1010
aat ttc tgc ctg ggg ccc tgt ccc tac atc tgg agc cta gac act cag Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln 335 340 345	1058
tac agc aag gtc ctg gct ctg tac aac cag cac aac ccg ggc gcg tcg Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser 350 355 360	1106
gcg gcg ccg tgc tgc gtg ccg cag gcg ctg gag cca ctg ccc atc gtg Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val 365 370 375 380	1154

tac tac gtg ggc cgc aag ccc aag gtg gag cag ctg tcc aac atg atc 1202  
Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile  
385 390 395

gtg cgt tcc tgc aag tgc agc tga ggccccgccc cgccacagc cccgcccacc 1256  
Val Arg Ser Cys Lys Cys Ser  
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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser  
210 215 220

Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Asp Tyr Lys Asp Asp  
275 280 285

Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys  
290 295 300

Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly  
305 310 315 320

Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu  
325 330 335

Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val  
340 345 350



Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys  
 355 360 365

Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly  
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Lys Cys Ser

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49

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ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg 30 35 40 45			145
atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser 50 55 60			193
ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val 65 70 75			241
ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val 80 85 90			289
gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr 95 100 105			337
cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys 110 115 120 125			385
ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg 130 135 140			433
gaa gcg gtg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg Glu Ala Val Pro Glu Pro Val Leu Ser Arg Ala Glu Leu Arg Leu 145 150 155			481
ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys 160 165 170			529
tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc Tyr Ser Asn Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro 175 180 185			577
agt gac tca ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg Ser Asp Ser Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg 190 195 200 205			625
cag tgg ctg acc cgc aga gag gct ata gag ggt ttt cgc ctc agt gcc Gln Trp Leu Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala 210 215 220			673
cac tct tcc tct gac agc aaa gat aac aca ctc cac gtg gaa att aac His Ser Ser Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn 225 230 235			721
ggg ttc aat tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg Gly Phe Asn Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met 240 245 250			769

aac cgg ccc ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag	817
Asn Arg Pro Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln	
255 260 265	
cac ctg cac agc tcc cgg cac cgc cga gcc ctg gat acc aac agc tac	865
His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr	
270 275 280 285	
cca tac gac gtg cca gac tac gca tct ctg gcc ctg gat acc aac tac	913
Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr	
290 295 300	
tgc ttc agc tcc acg gag aag aac tgc tgc gtg cgg cag ctc tac att	961
Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile	
305 310 315	
gac ttc cgg aag gac ctg ggc tgg aag tgg att cat gaa ccc aag ggc	1009
Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly	
320 325 330	
tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc tac atc tgg agc cta	1057
Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu	
335 340 345	
gac act cag tac agc aag gtc ctg gct ctg tac aac cag cac aac ccg	1105
Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro	
350 355 360 365	
ggc gcg tcg gcg gcg ccg tgc tgc gtg ccg cag gcg ctg gag cca ctg	1153
Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu	
370 375 380	
ccc atc gtg tac tac gtg ggc cgc aag ccc aag gtg gag cag ctg tcc	1201
Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser	
385 390 395	
aac atg atc gtg cgt tcc tgc aag tgc agc tga ggccccgccc cgccccacagc	1254
Asn Met Ile Val Arg Ser Cys Lys Cys Ser	
400 405	
cccccccacc cggcaggccc ggccccacccc ccgccccgcct caccgggggct gtattttaagg	1314
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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
 35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
 50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu  
 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
 100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
 115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
 130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
 145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
 165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
 180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
 195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser  
 210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp  
275 280 285

Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser  
290 295 300

Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg  
305 310 315 320

Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala  
325 330 335

Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln  
340 345 350

Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser  
355 360 365

Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val  
370 375 380

Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile  
385 390 395 400

Val Arg Ser Cys Lys Cys Ser  
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 Met Ala Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu  
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ccg ctg ctg tgg ctg cta gtg ctg acg cct ggc cgg ccg gcc gcc gga 97  
 Pro Leu Leu Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly  
 15 20 25

ctg tcc acc tgc aag acc atc gac atg gag ctg gtg aag cgg aag cgc 145  
 Leu Ser Thr Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg  
 30 35 40 45

atc gag gcc att cgc ggc cag att ctg tcc aag ctt cgg ctt gcc agc 193  
 Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser  
 50 55 60

ccc ccg agc cag ggg gac gtg ccg ccc ggc ccg ctg cct gag gca gta 241  
 Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val  
 65 70 75

ctg gct ctt tac aac agt acc cgc gac cgg gta gcc ggg gaa agt gtc 289  
 Leu Ala Leu Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val  
 80 85 90

gaa ccg gag ccc gag cca gag gcg gac tac tac gcc aag gag gtc acc 337  
 Glu Pro Glu Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr  
 95 100 105

cgc gtg cta atg gtg gaa agc ggc aac caa atc tat gat aaa ttc aag 385  
 Arg Val Leu Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys

110	115	120	125	
ggc acc ccc cac agc tta tat atg ctg ttc aac acg tcg gag ctc cgg				433
Gly Thr Pro His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg	130	135	140	
gaa gcg ctg ccg gaa cct gta ttg ctc tct cgg gca gag ctg cgc ctg				481
Glu Ala Val Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu	145	150	155	
ctg agg ctc aag tta aaa gtg gag cag cac gtg gag cta tac cag aaa				529
Leu Arg Leu Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys	160	165	170	
tac agc aat gat tcc tgg cgc tac ctc agc aac cgg ctg ctg gcc ccc				577
Tyr Ser Asn Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro	175	180	185	
agt gac tca ccg gag tgg ctg tcc ttt gat gtc acc gga gtt gtg cgg				625
Ser Asp Ser Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg	190	195	200	205
cag tgg ctg acc cgc aga gag gct ata gag ggt ttt cgc ctc agt gcc				673
Gln Trp Leu Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala	210	215	220	
cac tgt tcc tgt gac agc aaa gat aac aca ctc cac gtg gaa att aac				721
His Cys Ser Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn	225	230	235	
ggg ttc aat tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg				769
Gly Phe Asn Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met	240	245	250	
aac cgg ccc ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag				817
Asn Arg Pro Phe Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln	255	260	265	
cac ctg cac agc tcc cgg cac cgc cga gcc ctg gat acc aac agc tac				865
His Leu His Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr	270	275	280	285
cca tac gac gtg cca gac tac gca tct ctg gcc ctg gat acc aac tac				913
Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr	290	295	300	
tgc ttc agc tcc acg gag aag aac tgc tgc gtg cgg cag ctc tac att				961
Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile	305	310	315	
gac ttc cgg aag gac ctg ggc tgg aag tgg att cat gaa ccc aag ggc				1009
Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly	320	325	330	
tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc tac atc tgg agc cta				1057
Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu	335	340	345	
gac act cag tac agc aag gtc ctg gct ctg tac aac cag cac aac ccg				1105
Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro	350	355	360	365

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cont

ggc gcg tcg ccg gcg ccg tgc tgc gtg ccg cag gcg ctg gag cca ctg 1153  
Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu  
370 375 380

ccc atc gtg tac tac gtg ggc cgc aag ccc aag gtg gag cag ctg tcc 1201  
Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser  
385 390 395

aac atg atc gtg cgt tcc tgc aag tgc agc tga ggccccgccc cgcccacagc 1254  
Asn Met Ile Val Arg Ser Cys Lys Cys Ser  
400 405

cccgcccacc cggcaggccc ggccccacccc ccgcccgcct caccggggct gtattttaagg 1314

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Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr  
20 25 30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala  
35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser  
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu  
65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu



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Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu  
100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  
115 120 125

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val  
130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu  
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn  
165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser  
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu  
195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser  
210 215 220

Cys Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn  
225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His  
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp  
275 280 285

Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser  
290 295 300

Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg  
305 310 315 320

Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala  
325 330 335

Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln  
340 345 350

Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser  
355 360 365

Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val  
370 375 380

Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile  
385 390 395 400

Val Arg Ser Cys Lys Cys Ser  
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